

requested.

REMARKS/ARGUMENTS

In the response filed March 12, 2009, applicant provided a detail discussion of the rejections of record and arguments as to why the newly presented amended claims were distinguishable over the prior art relied upon and why the claims as amended were patentable thereover. Applicant therefore requests reconsideration of those arguments and remarks in light of the amended claims.

Election/Restriction

Examiner maintained the election/ restriction rejection stating that there is no evidence on record that the water miscible organic solvents enlisted are obvious variants of each other.

Applicants would like to bring to the attention of the Office (through the Examiner) that Independent claim 130 is directed to a process for extraction of insulin. The process includes treating expressed insulin present in bound form after the completion of fermentation with water miscible organic solvents selected from the group consisting of ethanol, isopropanol, t-butanol, acetic acid, dimethylformamide, dimethylsulfoxide, acetonitrile, dioxan, ethylene glycol, and propylene glycol.

Applicants have amended the claim 130 restricting water miscible organic solvents to a group selected from ethanol, isopropanol, acetic acid, dimethylformamide, dimethylsulfoxide, acetonitrile, dioxan, ethylene glycol, and propylene glycol. All of the enlisted solvents are miscible with water.

The selected solvents possess a common property i.e. water miscibility. Therefore, these solvents belong to the same group of water miscible organic solvents, which are polar in nature. (Abstract: Olofsson, L., Pernilla, S., Ian, N. Influence of water miscible organic solvent on α -chymotrypsin in solution and immobilized on Eupergit CM. Biotechnology Letters, Vol. 28, No. 12, June 2006,

pp. 929-935; Vollhardt KPC., Schore NE. Organic Chemistry Structure and Functions, 4th Edition, W.H. Freeman and Company, New York 2003; Page No. 228,249-250, 279, 280, 281; Lange, NA. Lange's Handbook of Chemistry. 13th Edition.McGraw-Hill Book Company; 10-103-116;
<http://virtual.yosemite.cc.ca.us/smurov/orgsoltab.htm>;
http://organicdivision.org/organic_solvents.html).

S. No.	Solvent	Formula	Solubility in water (g/100g)	Relative polarity
1.	Ethanol	C ₂ H ₆ O	Miscible	0.654
2.	Isopropanol	C ₃ H ₈ O	Miscible	0.546
3.	t-butanol	C ₄ H ₁₀ O	Miscible	0.389
4.	Acetic acid	C ₂ H ₄ O ₂	Miscible	0.648
5.	Dimethylformamide	C ₃ H ₇ NO	Miscible	0.404
6.	Dimethylsulfoxide	C ₂ H ₆ OS	Miscible	0.444
7.	Acetonitrile	C ₂ H ₃ N	Miscible	0.460
8.	Dioxan	C ₄ H ₈ O ₂	Miscible	0.164
9.	Ethylene glycol	C ₂ H ₆ O ₂	Miscible	0.790
10.	Propylene glycol	C ₃ H ₈ O ₂	Miscible	0.716
11.	Water	H ₂ O	Miscible	1

(Reference: <http://virtual.yosemite.cc.ca.us/smurov/orgsoltab.htm>)

The general rule of solubility (Solute-Solvent) or miscibility (solvent-solvent) states "like dissolve like". As the selected solvents are polar in nature and belong to the same group of polar solvent as water, these solvents are miscible with water. Thus, the selected water miscible organic solvents are obvious variants of each other in terms of water miscibility.

A prior art search for polar water miscible organic solvents will include the selected solvents. Further, restricting the claims to isopropanol will unnecessary limit the scope of the patent application as the present application enables the

extraction of insulin using all the specified solvents (Examples 1-2).

It is therefore evident from the facts and reasoning provided above that the claims have a single general inventive concept, i.e., the process for recovering insulin from culture medium/broth using water miscible organic solvents. Accordingly, reconsideration and withdrawal of the restriction requirement is respectfully requested.

I-Claim rejection - 35 USC § 102

As to the rejection of claims 130, 131, 135-137, 141 and 142 under 35 USC § 102(e) as being anticipated by Annibali (USPN 7,091,032), applicant would note the arguments presented in the response filed March 12, 2009.

Applicants would emphasize that Annibali teaches the addition of methanol to induce the expression of insulin in *Pichia*. Annibali teaches the addition of methanol to fermentation broth culture. Annibali, however, fails to describe or suggest the use of water miscible organic solvents that include ethanol, isopropanol, t-butanol, acetic acid, dimethylformamide, dimethylsulfoxide, acetonitrile, dioxan, ethylene glycol, and propylene glycol to extract the insulin present in bound form from the cells. Applicants have recognized that insulin present in the bound form in cells can be extracted with water miscible organic solvents such as the ones disclosed in the present process. Unlike the process of Annibali, the present invention teaches the use of water miscible organic solvents to extract the insulin present in the bound form from the cells.

In fact, Annibali does not even mention or recognize the presence of bound insulin in the expressing cells. Annibali does not teach or suggest the extraction of this bound insulin present in the expressing cells with water miscible organic solvents.

Accordingly, applicant requests reconsideration and withdrawal of this rejection.

II. Claim rejections - 35 USC § 103

Rejection based on over US 7,091,032 (Annibali) in view of Willis

(Modern Drug Discov., 2001, 4, 43-44)

As to the rejection of claim 140 under 35 USC § 103(a) as being unpatentable over Annibali (USPN 7,091,032), as applied to claims 130, 131, 135-137, 141 and 142 above, in view of Willis (Modern Drug Discov., 2001, 4, 43-44), applicant would again refer to the arguments and discussion set forth in the response filed March 12, 2009.

As noted the presently amended claim 130 is directed to a process for extraction of insulin. The process includes treating expressed insulin, which is present in bound form after the completion of fermentation in expressing cell, with water miscible organic solvents selected from the group consisting of ethanol, isopropanol, t-butanol, acetic acid, dimethylformamide, dimethylsulfoxide, acetonitrile, dioxan, ethylene glycol, and propylene glycol. The extraction of bound insulin using water miscible organic solvents results in overall increase in the yield of insulin.

Annibali does not teach this process and the other references relied upon do not provide a reason or basis to modify Annibali in a manner which would have reasonably led to the present invention.

In summary, neither Annibali nor Willis, taken separately or in combination, disclose a process for extraction of insulin, wherein the process includes treating expressed insulin present in bound form after the completion of fermentation with water miscible organic solvents selected from the group consisting of ethanol, isopropanol, t-butanol, acetic acid, dimethylformamide, dimethylsulfoxide, acetonitrile, dioxan, ethylene glycol, and propylene glycol.

Reconsideration and withdrawal of this rejection is therefore requested.

Examiner rejected the claims 132 and 133 under 35 USC § 103(a) as being unpatentable over Annibali (USPN 7,091,032), as applied to claims 130, 131, 135-137, 141 and 142 above in further view of Scopes et al. (Protein Purification: principles and Practice, Springer, new York, 1994, pp 157-71) and Gerlough & Bates (J. Pharm. Exp. Therapeutics, 1932, Vol. XLV, No. 1, pp. 19-51).

In response, applicants would again refer to the arguments and discussion relating to this rejection as set forth in the response filed March 12, 2009. In that response, applicants discuss this ground of rejection in light of the newly amended claims and demonstrates how the presently claimed invention distinguishes over the references herein relied upon.

In summary, neither Annibali, Scopes nor Gerlough and Bates, taken separately or in combination, disclose a process for extraction of insulin, wherein the process includes treating expressed insulin present in bound form after the completion of fermentation with water miscible organic solvents selected from the group consisting of ethanol, isopropanol, t-butanol, acetic acid, dimethylformamide, dimethylsulfoxide, acetonitrile, dioxan, ethylene glycol, and propylene glycol. Accordingly, claim 130 and dependent claims 132 and 133 are allowable over Annibali, Scopes, and Gerlough and Bates taken separately or in combination.

The references relied upon fail to provide an adequate basis in evidence to support the Examiner's initial conclusion of obviousness. In short there must be more than merely establishing that the individual components exist in the prior art. There must be something, found in the prior art which would have suggested, led or motivated one skilled in this art to bring those individual components together in the manner presently claimed. The present rejection lacks this aspect.

It is respectfully requested that this ground of rejection be reconsider and withdrawn.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance and notification to that effect is earnestly requested. If desired, the examiner is invited to conduct a telephone conference to expedite the prosecution of the subject application. In such a case, the examiner is invited to call the undersigned attorney.

Should any official at the United States Patent and Trademark Office deem that any further action by the Applicant or Applicant's undersigned representative is desirable and/or necessary, the official is invited to telephone the undersigned at the number set forth below.

The Commissioner is hereby authorized to charge any fees which may be required regarding this application under 37 CFR §§ 1.16-1.17 or credit any overpayment, to deposit account No. 503321. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, or otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 503321.

Respectfully submitted,

By: Sam Zaghmout

O. M. (Sam) Zaghmout Ph.D
(Registration No. 51,286)

Contact Information:

Bio Intellectual Property Service (BIO IPS) LLC

8509 Kernon Ct, Lorton, VA 22079. USA

Cell Phone (703-919-4348), Fax: (703-550-0409), (703) 550-1968 (Voice/Fax)